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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/809,773	03/16/2001	Frederick M. Ausubel	00786/380002	8780

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EXAMINER
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PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 07/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/809,773

Applicant(s)

AUSUBEL ET AL.

Examiner

Scott D. Priebe

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 21 June 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

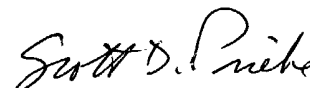
The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-7, 17-25, 27, 28 and 30.Claim(s) withdrawn from consideration: 8-16, 29 and 31-39.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☒ Other: PTO-892 attached.



Scott D. Priebe  
Primary Examiner  
Art Unit: 1632

Continuation of 3. Applicant's reply has overcome the following rejection(s): the rejection of claims 1-7 under 35 USC 101, the rejection of claim 27 under 35 USC 112, 2nd para..

Continuation of 5. does NOT place the application in condition for allowance because:

With respect to the rejection for lack of adequate written description for a generic nematode persistently infected with generic bacteria, as defined in the specification (pages 5-6), "persistently infected" requires that the bacteria be damaging to the nematode, i.e. be pathogenic to the nematode (as opposed to being pathogenic in humans). Applicant argues that a large variety of nematode species were known to those of skill in the art, and that nematodes possess common attributes, and therefore description of one nematode, *C. elegans*, would provide sufficient description for the claimed genus. However, as Applicant notes, classification of nematodes "is largely based on morphology." There is no evidence of record to suggest that their response to infection by various bacteria is a common attribute. Furthermore, the issue is not whether one of skill knew of a large variety of nematode species, but whether Applicant was in possession of a generic nematode "persistently infected" with generic bacteria based upon disclosure of a single species readable on the invention. Applicant states (page 10) that persistent infection is an artificial relationship, and Applicant was unaware of any report of persistent infection in nature. This suggests that one of skill in the art would also be unaware of persistently infected nematodes, and if "persistent infection" requires hand of man to produce, then one of skill would be unaware a priori of what bacteria would produce persistent infection in what nematode, i.e. possession would not be achieved until the persistently infected nematode had been made. The specification does not identify a single "persistently infected" nematode other than *C. elegans* that is persistently infected with *S. typhimurium*, nor does it describe what bacteria would persistently infect what other nematodes. Applicant has argued that while *P. aeruginosa* is pathogenic to *C. elegans*, it does not "persistently infect" *C. elegans*, as defined. However, as explained below, Tan (Jan. 1999) presents evidence that *P. aeruginosa* does "persistently infect" (as defined) *C. elegans*. It is unclear how one would reconcile Applicant's statement with the results of Tan (Jan. 1999). Furthermore, Bottjer et al. (Amer. J. Veterin. Res. 39 (1): 151-153, 1978) discloses that the parasitic nematode *Nematospiroides dubius* may be a carrier of *S. typhimurium* in nature. The success in growing infected *N. dubius* suggests that *N. dubius* is not harmed by *S. typhimurium*, i.e. the infection does not meet the definition of persistently infected. Bottjer also discloses that parasitic helminths (roundworms) in general were known to be carriers of pathogenic Enterobacteriaceae, which appear to be pathogenic to *C. elegans*. Consequently, simply because nematodes are "simply roundworms" with known common attributes, does not mean that the known common attributes extend to whether persistent infection with a given pathogen in *C. elegans* is predictive of a pathogen that will be pathogenic to other nematodes.

With respect to the enablement rejection, Applicant points to the disclosure on pages 11-13, 20-25 of the specification as providing guidance for the invention as broadly claimed. However, this disclosure deals strictly with *C. elegans* infected with *S. typhimurium* or *P. aeruginosa*, or feeding on *E. coli*. Applicant asserts that one of skill in the art would recognize that any nematode may be employed, and suggests that one need merely to culture the nematode in the presence of the bacteria and then determine whether the nematode became persistently infected, and that such unguided (as to identity of specific nematode and bacterium) trial and error experimentation would not be undue. However, as set forth in *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), compliance with 35 USC 112, first paragraph requires: "that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." As applicant has stated, they were unaware of reports of "persistent infection" of nematodes in nature, although as shown by Bottjer those in the art were aware of non-pathogenic infection, which does not meet Applicant's definition of "persistent infection". The only prior art identified by the Office as readable on the invention involves persistent infection of *C. elegans* with *P. aeruginosa*, however Applicant indicates this is not "persistent infection". Taken together, this suggests that one of skill in the art could not predict what bacterium would persistently infect what nematode, and the trial and error experimentation required to practice the invention as broadly claimed would be undue.

With respect to the rejections under 35 USC 102(b) over Tan or Ausubel, Applicant argues that neither reference anticipates the claims because they do not disclose *C. elegans* "persistently infected," as defined on pages 5-6, with *P. aeruginosa*. Applicant argues that the results disclosed in the instant specification (page 12, lines 12-17) show that *P. aeruginosa* does not establish a persistent infection because the experiment described on pages 11-12 did not result in death of *C. elegans* following a 6 hour growth on *P. aeruginosa* followed by growth on *E. coli*. However, the definition of "persistent infection" does not require the infection to be fatal. It requires that the number of bacteria infecting the nematode not fall below 30% of the number present before shifting to a non-infectious environment. Furthermore, Tan et al. (Proc. Natl. Acad. Sci. USA, 96: 715-720, Jan. 1999), which is reference 2 cited in Tan et al. (PNAS 96: 2408-2413, 1999) disclosed (page 718) that growth of *C. elegans* on *P. aeruginosa* for 18, 24 or 30 h under slow killing conditions, before switching to growth on *E. coli*, led to death of 25%, 70%, and 95%, respectively, of the *C. elegans* by 60 h growth on *E. coli*. Growth on *P. aeruginosa* for under 12 h before switching to growth on *E. coli* was not lethal, so it is not surprising that growth on *P. aeruginosa* for 6 hr did not result in persistent infection. The results in Tan combined with the results with *S. typhimurium* and *P. aeruginosa* described in the instant specification suggest that *S. typhimurium* is more pathogenic in *C. elegans*, not that *P. aeruginosa* does not persistently infect *C. elegans*.